# Khondrion highlights potential role of inflammatory lipid modulator prostaglandin E2 in COVID-19 disease and proposes potential treatment pathway with sonlicromanol

*Elevated levels of $PGE_2$ known to play an essential role in inflammation*

*Inhibition of key enzyme involved in $PGE_2$ production may offer a potential new treatment approach in protecting COVID-19 patients from severe disease progression and death*

*Company's lead asset sonlicromanol may have potential as a repurposed treatment for $PGE_2$-driven inflammatory consequences underlying severe COVID-19 disease*

NIJMEGEN, the Netherlands – Wednesday April 15, 2020: Khondrion, a clinical-stage pharmaceutical company discovering and developing therapies targeting mitochondrial disease, has published a scientific hypothesis that the inflammatory lipid modulator, prostaglandin E2 ($PGE_2$), may execute a prominent role in COVID-19 pathophysiology and proposes that its lead drug candidate, sonlicromanol, currently in phase IIb development to treat a range of mitochondrial diseases, could be repurposed for the treatment of patients with severe COVID-19 disease.

The paper, published online by *Preprints*, the online multidisciplinary platform dedicated to making early versions of research outputs permanently available and citable, summarizes the potential role that elevated levels of $PGE_2$, which is known to play an essential role in inflammation[1] and defense against infectious agents[2], may have in COVID-19 pathology. It calls for the measurement of $PGE_2$ in affected patients and proposes selective inhibition of a key enzyme involved in $PGE_2$ production – microsomal prostaglandin E synthase-1 (mPGES-1) – as a potential new treatment approach in protecting COVID-19 patients from severe disease progression and death.

inflammatory drugs (NSAIDs) and COX-2 inhibitors[3]. The Khondrion research team's hypothesis that selective mPGES-1 inhibition might reduce COVID-19 associated disease symptoms, e.g. acute respiratory distress syndrome (ARDS), is based on $PGE_2$'s role as an inflammatory modulator in viral infections as well as evidence that targeted $PGE_2$ inhibition enhances antiviral immunity[4,5,6].

Sonlicromanol, Khondrion's wholly-owned investigational lead asset currently in phase IIb development as a potentially disease-modifying treatment for mitochondrial disease, has a triple mode of action that includes the inhibition of mPGES-1 and may, in turn, result in an anti-inflammatory effect. Khondrion research using human fibroblast cells and a mouse macrophage-like cell line shows that sonlicromanol is able to block mPGES-1 and decrease $PGE_2$ production. Therefore, in addition to it being a novel therapeutic option for mitochondrial disease patients, the Company proposes that sonlicromanol may also have potential to be repurposed to treat $PGE_2$-driven inflammatory consequences that might underly COVID-19 associated ARDS or, when administered early after diagnosis, might prevent progression to ARDS.

**Prof. Dr. Jan Smeitink, Chief Executive Officer at Khondrion, said:** *"During the development of sonlicromanol for the treatment of mitochondrial disease we have generated a wealth of data on its mode of action, including its effects on the body's inflammatory responses. What we have learned about this asset's potential is striking when examined through the lens of COVID-19 and the scientific community's search for new therapies as part of the global response to this pandemic.*

*"While there remain limitations in our understanding of $PGE_2$ and its role in the serious lung disease associated with COVID-19, we believe it warrants further investigation, particularly when new therapeutic options are so desperately needed.*

*"We are inviting experts in the field of coronavirus to test our compound in-vitro and in-vivo. We are also actively searching for partners willing to assist us in evaluating our hypothesis and the potential of bringing sonlicromanol to COVID-19 patients."*

The paper **"Hypothesis: mPGES-1-derived Prostaglandin E2, a so far missing link in COVID-19 pathophysiology?"** is available on Preprints here.

**References**

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**About Khondrion**

Khondrion is a clinical-stage pharmaceutical company discovering and developing therapies targeting mitochondrial disease. Founded by Prof. Jan Smeitink, a world-leader in mitochondrial medicine, the company is advancing its proprietary science through a wholly-owned clinical and preclinical small molecule pipeline of potential medicines. Khondrion is headquartered in Nijmegen, The Netherlands. For more information visit www.khondrion.com

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